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(19)(CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Licidal and Lice-Ovicidal Pharmaceutical and Cosmetic Formulations

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LICIDAL AND LICE-OVICIDAL PHARMACEUTICAL AND COSMETIC FORMULATIONS.

FIELD OF INVENTION

The present invention relates to pharmaceutical and cosmetic preparations, and more specifically, to a novel chemical formulation containing the active ingredient d-LIMONENE, ~~for~~ use in the eradication of lice and lice eggs.

BACKGROUND OF THE INVENTION

The prior art has identified the use of d-LIMONENE as an effective active ingredient against fleas, however, experiments recorded in the literature and field tests performed by the inventor clearly show the ineffectiveness of d-LIMONENE against flies and mosquitoes.

The prior art has not identified the use of d-LIMONENE as an active ingredient in the destruction and/or prevention of lice in their various stages of development.

Lice and lice egg infestation is a major problem affecting large segments of the population, both children and adults. The commercially available preparations and treatments are generally dangerous to the eyes, so that they must be very carefully applied to the head, since they have a high toxicity level.

Therefore, it would be desirable to provide a medical preparation which is effective in the eradication of lice and lice eggs, which is easy to apply, and which can be formulated in various ways, with a low toxicity.

SUMMARY OF THE INVENTION

The invention discloses a licidal and lice-ovicidal formulation using d-LIMONENE as an active ingredient in pharmaceutical preparations for the destruction and/or prevention of lice, located on the head, on the

human body or thereabout (bedding, sheets), or on animals or thereabout.

The inventive novelty resides in the discovery of the use of d-LIMONENE against lice as the most effective material, which has a relatively very low toxicity, as compared with preparations and medications now in use.

The inventive preparations can take the form of shampoo, spray, foam, cream and the like for treatment of lice.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

The substance d-LIMONENE is a naturally occuring monoterpene, and is an organic material found in many volatile oils, especially citrus oils, or is derived from essential citrus oils, through refinement processes and/or extraction. The major quantities of d-LIMONENE available today are obtained from essential oils derived from citrus fruit peels, mainly from orange peels, which provides orange oil. It is a material used as a flavor and fragrance additive for household cleaning products, as an industrial solvent, and in the food and cosmetic industries.

The chemical formulation for d-LIMONENE is $C_{10}H_{16}$, and has a molecular weight of 136.2, and specific gravity, at 25° C, of .836 to.843. It is also known by the chemical names LIMONENE, 1,8(9) P-Menthadiene, and 1-Methyl, 4-Isopropenyl, 1-Cyclohexene. The structural formula of d-LIMONENE can be represented as:

Other specifications of the substance d-LIMONENE appear in the circular published by the Essential Oil Association of USA, Inc., E.O.A. No. 253.

Experiments using preparations containing the chemical

achieved in eradication of lice and lice eggs. The principle of the invention is in the use of d-LIMONENE in preparations and medications for treatment of lice located on the head, on the human body and thereabout, and on animals.

The preparations and medications for treatment of lice may be provided in the form of shampoo, spray with solutions, foam, cream, liquid, powder, lotion, vapor, solid, etc.

The percentage of d-LIMONENE in the preparations and medications can be established in accordance with the type of treatment, the extent of the lice infestation and the area affected, and the type and age of the individual being treated. The percentage may vary from 0.01% to 60%.

The aforementioned preparations and medications for treatment of lice generally contain additional materials for purposes of preserving the active ingredient, preserving the shelf life of the products, and additional materials to nourish and preserve the health of the treated area.

The additional materials include generally accepted types, such as preservatives, solutions, water, fragrance material, foaming agents, and materials for preserving the health of the affected area, carrier material and emulsifiers, etc.

Experiments conducted by the inventor with lice and lice eggs surprisingly revealed d-LIMONENE as being unusually effective against lice, and lice eggs, when mixed in solutions such as water and alcohol.

The experiments were divided into two stages, the first stage performed on children between the ages of 5-10, using shampoo with d-LIMONENE. The second stage was performed at Hadassah Hospital, Ein Kerem, Jerusalem, Israel, with shampoo and with alcohol and d-LIMONENE under laboratory conditions. The experimental results are presented and discussed.

First Stage

The preparation which was tried was a regular shampoo mixed with d-LIMONENE in various percentages, as shown in Table I of the experimental results. The shampoo was applied to the heads of children between the ages of 5-10. All of the children were clearly infested with lice and a count was made of the lice and lice eggs before the shampoo application and after.

The children chosen for the experiment had generally light colored hair, to enable easier examination of the amount of lice and lice egg infestation. The examination was made by observation under a magnifying glass, in an exact manner before and after the shampoo application.

The heads of the children were washed before the treatment, and the hair was scrubbed with shampoo during 3 minutes in a thorough fashion, such that the shampoo came into contact with all of the hair, hair roots and scalp. After the shampoo application, the children's hair was washed for 3 minutes with water until all of the shampoo was completely removed. The treatment was performed with water at a temperature of 38-40° Centigrade. No lice comb was used during the treatments, nor comb or brush, nor any other means during the shampoo application or after. The same shampoo was used for each stage of the experiment. The experiment was performed in June 1989.

TABLE I

CHILD NUMBER	% d-LIMONENE IN SHAMPOO	QUANTITY BEFORE SHAMPOO		QUANTITY AFTER SHAMPOO	
		LICE	LICE EGGS	LICE	LICE EGGS
1	0%	55	100	40	90
2	0%	65	90	55	85
3	1%	70	120	5	30
4	1%	55	90	4	25
5	2%	80	110	0	15

	7	4%	100	150	0	3
	8	4%	80	110	0	1
	9	5%	70	100	0	0
	10	5%	65	110	0	0

Second Stage

The second stage was performed in the laboratory of Hadassah Hospital, Ein Kerem, Jerusalem. The second stage was performed with lice and lice eggs grown under laboratory conditions. The lice used in the experiment were fed during 24-48 hours on lice-infested rabbits. The experiment was performed with 25 female and 25 male lice, for a total of 50 in each experiment.

The lice eggs used in the experiment were grown on human hair for 2-6 days. The experiment used 50 eggs each time.

The experiment was performed on round filter paper of 7 cm diameter. The lice and lice eggs were applied to the filter paper and were exposed to 1 gram of the formulation for 15 minutes. The filter paper was then washed in water for 1 minute after the experiment, and then placed in isolation for 12 hours. After, the results were checked, and these are listed in Table II.

The experiment was performed with shampoo mixed with various percentages of d-LIMONENE, and with alcohol mixed with various percentages of d-LIMONENE.

One of the reasons for checking the effectiveness with alcohol was as a control experiment, and to achieve better contact of the lice and lice eggs on the filter paper, since it was not possible to scrub the lice with shampoo on the filter paper as was done in the first stage. The contact between the shampoo with d-LIMONENE and the lice is less effective than the shampoo application, because of the form of the shampoo (jelly).

The second stage of the experiment itself was performed to obtain a clear indication of the mortality of lice and lice eggs, using preparations with d-LIMONENE, so as to remove any doubt that in the first stage, the lice and lice eggs were washed from the childrens' heads, without conclusive evidence of mortality. The experiment was performed in September 1990.

TABLE II

d-LIMONENE % IN SHAMPOO	%MORTALITY OF LICE AFTER 12 HOURS	% MORTALITY OF LICE EGGS AFTER 12 HOURS
0%	16%	0%
1%	22%	10%
5%	38%	22%
10%	46%	35%
20%	70%	55%
40%	96%	90%

d-LIMONENE % IN ALCOHOL	MORTALITY OF LICE AFTER 12 HOURS	% MORTALITY OF LICE EGGS AFTER 12 HOURS
0%	28%	6%
1%	90%	50%
5%	100%	70%
10%	100%	90%
20%	100%	99%

The beneficial effects of the preparations in their different formulations are in their ability to destroy and prevent lice and lice egg infestation, on the head, on the body and on animals, through external treatment which brings the preparation in contact with the infested area, for a certain time. The following are examples of the preparations, formulations and their contents, in four products: shampoo, foam, cream, and spray.

SHAMPOO INGREDIENTS Range of contents from	% to	%
d-LIMONENE	5%	40%
WATER	80%	45%
SODIUM LAURYL SULFATE	1%	4%
CITRIC ACID	1%	2%
AMINO ACID	2%	1%
COCAMIDO PROPYL BETAINE	4%	1%
2 - BROMO - 2 - NITROPROPANE - 1.3 - DIOL	0.5%	1%
ALKYL SULFATE	2%	3.5%
SODIUM CHLORIDE	3.5%	2%
PROPYLENE GLYCOL	1%	0.5%

FOAM INGREDIENTS Range of contents from	% to	%
d-LIMONENE	0.01%	40%
WATER	78.99%	39%
S. D. 40 ALCOHOL	2%	5%
VINYL PYRROLIDONE	5.5%	3%
ETHYL METHACRYLATE	3%	5%
OLEIC ACID	5%	3%
VINYL ACETATE	2.5%	2%
PROPYLENE GLYCOL	2%	2.5%

CREAM INGREDIENTS Range of contents from	%	to %
d-LIMONENE	1%	30%
WATER	60%	45%
MINERAL OIL	19%	5%
ISOPROPYL MYRISTATE	4%	6%
PROPYLENE GLYCOL	6%	4%
GLYCERYL STEARATE	2%	1%

LAUROAMPHOGLY ATE	2%	
SODIUM LAURYL SULFATE	1%	2%
ISOSTEARYL ALCOHOL	3%	1%
P. E.G. - 40 STEARATE	1%	2%
CETYL ALCOHOL	1%	3%

SPRAY INGREDIENTS Range of contents from	%	to %
d-LIMONENE	10%	60%
S. D. 40 ALCOHOL	70%	20%
WATER	5%	10%
PROPYLENE GLYCOL	4%	1%
ISOPROPYL MYRISTATE	1%	4%
P. E. G. - 40 STEARATE	10%	5%

These examples can be produced in different and/or similar combinations, in forms such as shampoo foam, cream, liquid and aerosol, etc.

While certain representative embodiments and details have been shown for the purpose of illustrating this invention, it will be apparent to those skilled in the art that various changes and modifications can be made there in without departing from the scope of this invention.

PROPERTY OR PRIVILEGE IS CLAIMED ARE AS FOLLOWS:

1. A medical preparation for destroying and preventing lice and lice egg infestation, comprising the active ingredient d-LIMONENE and carrier materials.

2. The preparation of claim 1 wherein the concentration of d-LIMONENE comprises between 0.01% to 60%.

3. The preparation of claim 1 for destroying and preventing lice and lice egg infestation on the head and human body and thereabout.

4. The preparation of claim 1 for destroying and preventing lice and lice egg infestation on animals and thereabout.

5. The preparation of claim 1 further comprising at least one of alcohol, water and other solvents, preservatives, foaming agents, carrier materials, and emulsifiers.

6. The preparation of claim 1 provided as a foam.

7. The preparation of claim 1 provided as a cream.

8. The preparation of claim 1 provided as a spray.

9. The preparation of claim 1 provided as a shampoo.

10. The preparation of claim 1 provided as a liquid.

11. The preparation of claim 1 provided as an aerosol.

12. The preparation of claim 1 provided as a powder.

13. The preparation of claim 1 provided as a lotion.

14. The preparation of claim 1 provided as a vapor.

15. The preparation of claim 1 provided as a solid.

16. A cosmetic preparation for destroying and preventing lice and lice egg infestation, comprising the active ingredient d-LIMONENE and carrier materials.

17. A method of producing a medical preparation for destroying and preventing lice and lice egg infestation, comprising the active ingredient d-LIMONENE and carrier materials, and comprising at least one of the steps of mixing, reactive processing, and refining using heating means, cooling means, and filling means.